

temperature of the insert] of 37°C for 16 hours in 5X SSC, 5X Denhardt solution, 25% formamide, and 100 µg/ ml denatured salmon sperm DNA, with washes in 2X SSC, 0.1% SDS at 25°C; 1X SSC, 0.1% SDS at 60°C; or 0.1X SSC, 0.1% SDS at 60°C;

- b) introducing the insert into a recombinant cloning vector;
- c) introducing said vector into a competent cellular host; and
- d) recovering the DNA recombinants.

REMARKS

Reconsideration of this application is respectfully requested.

Claims 90, 92, 99, and 101 have been amended to provide exemplary hybridization and wash conditions corresponding to conditions of 42°C below the melting temperature, 20°C below the melting temperature, and 3°C below the melting temperature. The amendments are fully supported by the specification, for example, on page 35, paragraph 2, and page 38, paragraph 2. No new matter enters by amendment.

Claims 90-109 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention at the time the application was filed. The Office contends that the specification only provides a limited number of subgenomic HIV-2 clones, and that the specification fails to provide sufficient guidance pertaining to the nucleotide sequence of

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the inserts within these clones, with the exception of the LTR, *gag*, and *pol* [sic, *env*] genes described on pages 56-61 and Figures 6 and 7. The Office further contends that the specification fails to provide the hybridization parameters that should be employed, and that melting temperatures are only disclosed with regard to HIV-1 probes. The Office concludes that the specification does not provide any guidance pertaining to the identification, isolation, preparation, and use of HIV-2 specific probes under the claimed hybridization conditions. The Office cites case law in support of the contention that an adequate description of DNA requires a nucleotide sequence. Applicants traverse the rejection.

The test for sufficiency of support in an application is whether the disclosure reasonably conveys to the artisan that the inventor had possession of the claimed subject matter at the time of filing. Ralston Purina Co. v. Far-Mar-Co., Inc., 772 F.2d 1570, 1575, 227 U.S.P.Q. 177, 179 (Fed. Cir. 1985). In making this determination, the specification as a whole must be considered. In re Wright, 866 F.2d 422, 424, 9 U.S.P.Q. 2d 1649, 1651 (Fed. Cir. 1989).

At the time the application was filed, applicants had possession of **methods** for producing HIV-2 probes and for detecting HIV-2 nucleic acids. Upon reading the specification as a whole, the skilled artisan would conclude that applicants had possession of the claimed **methods**.

For example, the specification describes using the lambda ROD 4 recombinant containing the total cDNA of HIV-2 as a probe under the low stringency conditions of

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Example II. (Specification at page 38, paragraph 2). Example II describes hybridization conditions of 37°C for 16 hours in 5X SSC, 5X Denhardt solution, 25% formamide, and 100 µg/ ml denatured salmon sperm DNA (Tm -42°C). (Specification at page 35, paragraph 2). These hybridization conditions are recited in the amended claims. The specification describes washing hybridizations with the lambda ROD 4 recombinant containing the total cDNA of HIV-2 successively in 2X SSC, 0.1% SDS at 25° (Tm -42°C); 1X SSC, 0.1% SDS at 60° (Tm -20°C); and 0.1X SSC, 0.1% SDS at 60° (Tm -3°C). (Specification at page 38, paragraph 2). These washing condition are recited in the amended claims. Thus, contrary to the Office's assertion, the recited hybridization and wash conditions are disclosed with regard to hybridization with HIV-2 probes.

The specification describes dot-blot hybridization of a 2 kilobase HIV-2 probe to HIV-2 nucleic acid under stringent conditions. (Specification at page 40, paragraph 1, and pages 42-43, bridging paragraph). 11 of 11 isolates were identified as HIV-2 using this method. Id. The specification further describes that the invention relates to a DNA or RNA capable of hybridizing with HIV-2 DNA or RNA under non-stringent conditions. (Specification at 50, paragraph 1). The specification also describes that preferred embodiments include detecting HIV-2 nucleic acids under stringent and non-stringent conditions. (Specification at page 54, line 2, through page 55, line 4). Consequently, the skilled artisan would recognize that hybridization and wash conditions **recited in the specification** (i.e. hybridization at 37°C for 16 hours in 5X SSC, 5X Denhardt solution, 25% formamide, and 100 µg/ ml denatured salmon sperm DNA, with washes in 2X SSC,

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0.1% SDS at 25°; 1X SSC, 0.1% SDS at 60°; or 0.1X SSC, 0.1% SDS at 60°) would be within the scope of the invention.

The written description requirement may be satisfied if the broader concept would naturally occur to one skilled in the art upon reading the earlier specification. In re Smythe, 480 F.2d 1376, 1384, 178 U.S.P.Q. 279, 285 (C.C.P.A. 1973). The specification describes the total cDNA of HIV-2 and provides restriction maps of HIV-2. (Specification at Figs. 4-8). The specification describes subgenomic clones of HIV-2, which together reconstitute the complete HIV-2 ROD genome. (Specification at 26, lines 14-23.) Therefore, applicants describe clones encompassing the entire genome of HIV-2. Consequently, the skilled artisan would recognize that applicants possessed HIV-2 probes that are capable of hybridizing to **any** region of the HIV-2 genome using the claimed methods.

In addition, sequences of *gag*, *env*, and LTR regions are described. (Specification at 68-88). Having read the specification, the skilled artisan would recognize that applicants possessed many different HIV-2 probes that could be used in the claimed methods, including the lambda ROD 4 recombinant containing the total cDNA of HIV-2 and subgenomic fragments of HIV-2. The concept of using probes from any region of HIV-2 for producing HIV-2 probes and detecting HIV-2 nucleic acids under stringent and non-stringent conditions would naturally occur to the skilled artisan.

The Office has provided no explanation of why the claimed **methods** are not described in the specification as required to support a rejection under 35 U.S.C. § 112,

first paragraph. See In re Wertheim, 541 F.2d 257, 265, 191 U.S.P.Q. 90, 98 (C.C.P.A. 1976). Instead, the Office appears to require that applicants provide a nucleotide sequence of all probes that can be used in the claimed **methods**. Applicants submit that the focus of the inquiry should not be not whether applicants have described every probe that can be used in the claimed **methods**, but whether applicants have described the claimed **methods**. Applicants need not describe all species that a claim encompasses to fulfill the written description requirement. Utter v. Hiraga 845 F.2d 993, 998, 6 U.S.P.Q. 2d 1709, 1714 (Fed. Cir. 1988). Consequently, applicants need not provide the nucleotide sequence of all HIV-2 probes that can be used in the claimed methods.

The claimed methods are broadly applicable, and applicants have provided the requisite written description of these methods. The successful use of these methods is predictable. Applicants have provided exemplary probes for use in the claimed methods. For, example, applicants have described using the lambda ROD 4 recombinant containing the total cDNA of HIV-2 as a probe. Applicants also described using the 2 kilobase E2.1 HIV-2 insert as a probe. (See Specification at pages 32-34). Applicants described restriction maps of HIV-2 and DNA and amino acid sequences for Gag and Env proteins of HIV-2. Having read the specification, the skilled artisan would recognize that applicants possessed **methods** of producing and using HIV-2 probes that are capable of hybridizing to any region of HIV-2. Therefore, applicants have satisfied the written description requirement of 35 U.S.C. § 112, first paragraph.

In addition, original claims 37 and 41 recite methods of producing and using HIV-2 probes. Original claims 37 and 41 are dependent on original claims 28-36 and 27-35,

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respectively. Original claim 29 recites LTR sequences. Pending claims 92, 93, 101, and 102 recite these sequences. Original claims 30-33 recite a nucleic acid coding for at least part of several HIV-2 Gag amino acid sequences. Pending claims 92, 94-97, 101, and 103-106 recite these amino acid sequences. Original claim 34 recites a nucleic acid coding for at least part of an HIV-2 Env amino acid sequence. Claims 92, 98, 101, and 107 recite these amino acid sequences. Having read the original claims, the skilled artisan would recognize that applicants invented the methods encompassing a large genus of probes that could be used in the claimed methods.

Applicants have claimed methods in this application. Applicants have provided nucleotide sequences of a representative number of HIV-2 specific probes, which will work in the claimed invention. Furthermore, applicants have recited a common structural feature of the members of the genus of probes, which will work in the claimed methodology. Specifically, applicants have recited that the probes hybridize to HIV-2 ROD genomic DNA under hybridization conditions of 37°C for 16 hours in 5X SSC, 5X Denhardt solution, 25% formamide, and 100 µg/ ml denatured salmon sperm DNA, with washes in 2X SSC, 0.1% SDS at 25°C; 1X SSC, 0.1% SDS at 60°C; or 0.1X SSC, 0.1% SDS at 60°C. Applicants submit that this feature adequately describes the specific probes of the claimed invention. Accordingly, applicants submit that the requirements of the 35 U.S.C. § 112, first paragraph, have been fulfilled, and respectfully request withdrawal of the rejection.

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Applicants respectfully submit that this application is now in condition for allowance. If the Examiner should disagree, he is invited to contact the undersigned to discuss any remaining issues.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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By: 
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